CCCLXXX.—*The Halogenation of Phenolic Ethers and Anilides.** *Part I. The Bromination of Ethers in 50% Acetic Acid.*

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The study of the relative rates of chlorination of a number of substituted phenolic ethers has brought to light striking and unexpected regularities (Bradfield and Jones, J., 1928, 1006, 3073). Attention has now been directed to the relative rates of bromination at 20° of certain *p*-chloro- and *p*-bromo-phenyl ethers in a medium consisting of a mixture of equal volumes of glacial acetic acid and water (" 50% acetic acid "), and the existence of similar regularities is demonstrated.

The rates of interaction of bromine with organic substances have been measured by a number of workers, and it is found that the hydrobromic acid formed in oxidation and substitution reactions exerts a disturbing influence. A constant value for the velocity coefficient for such reactions is not obtained when, in the application

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of mass-law expressions, the concentration of the bromine is placed equal to the titratable bromine, because only that portion of the bromine " unfixed " as perbromide in the reversible reaction $Br_2 + Br' \rightleftharpoons Br_3'$ is active in substitution or oxidation reactions (Ramberg, *Z. physikal. Chem.*, 1900, **34**, 561; Bruner, *ibid.*, 1902, **41**, 513; Bugarszky, *ibid.*, 1901, **38**, 561; 1904, **48**, 63; 1910, **71**, 705; Bognár, *ibid.*, 1910, **71**, 705; Watson, J., 1928, 1137).

The existence of the perbromide equilibrium has been demonstrated by a diversity of methods, *viz.*, partition (Wildermann, *Z. physikal. Chem.*, 1893, **11**, 407; Roloff, *ibid.*, 1894, **13**, 341; Jakowkin, *ibid.*, 1896, **20**, 19), electrolytic (Boericke, *Z. Elektrochem.*, 1905, **11**, 57), aspiration (W. J. Jones, J., 1911, **99**, 392), and colorimetric (Joseph and Jinendradasa, *ibid.*, p. 274). The attainment of equilibrium in 50% acetic acid was shown by trial experiments to be extremely rapid from both sides; for example, on the addition of a solution of *p*-cresol to one of bromine containing ten molecular proportions of hydrobromic acid, only the merest trace of bromine can be detected after one minute.

The calculation of the velocity coefficients for the bromination of phenyl ethers is carried out as follows. For the comparatively slow reactions under examination, it follows from the experiments referred to above that in the changing system the concentration of " unfixed " bromine is always at its equilibrium value, and the relation between the " unfixed " and the total bromine concentrations is given by $K = [Br_2][Br']/[Br_3']$. There is no reason to doubt the validity of the concentration–equilibrium constant under the conditions of these experiments, namely, with 10 or 5 molecular proportions of hydrobromic acid present initially, so that the total concentration of this acid is only increased by 10% or 20% when the reaction is complete, and the use of this constant in the former case appears to be justified by the success of the calculation. Data for the alternative calculation of an activity-equilibrium constant are not available.

All concentrations are referred to g.-mols./litre. If a and b are the initial concentrations of bromine and hydrobromic acid, x is the concentration of bromine which has reacted with the ether after t minutes, and y the equilibrium concentration of " unfixed " bromine, the concentration of the perbromide ion is $(a - x - y)$, that of hydrobromic acid is $\{b + x - (a - x - y)\}$, and

$$2y = \sqrt{(K + b - a + 2x)^2 + 4K(a - x)} - (K + b - a + 2x).$$

The rate of reaction is :

$$dx/dt = k(c - x)y = \tfrac{1}{2}k(c - x)\{\sqrt{(K + b - a + 2x)^2 + 4K(a - x)} - (K + b - a + 2x)\} \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where c is the initial concentration of ether. The solution * to this equation is

$$\frac{ktK(c-a)}{2{\cdot}303} = (K+b+a)\log_{10}\frac{v_0}{v} + 2(c-a)\log_{10}\frac{2v_0+K}{2v+K} - (\alpha-p)\log_{10}\frac{v_0+\alpha+p}{v+\alpha+p} - (\alpha+p)\log_{10}\frac{v_0+\alpha-p}{v+\alpha-p}\,. \qquad (2)$$

where $v_0 = \frac{1}{2}\sqrt{(K+b-a)^2+4Ka} - \frac{1}{2}(K+b-a)$

$$v = \tfrac{1}{2}\sqrt{(K+b-a+2x)^2+4K(a-x)} - \tfrac{1}{2}(K+b-a+2x)$$

$$\alpha = \tfrac{1}{2}(K+2c+b-a)$$

$$p = \sqrt{\alpha^2-K(c-a)}.$$

The above method of allowing for the disturbing effect of hydrobromic acid closely resembles Bugarszky's treatment of the kinetics of the (oxidation) reaction between bromine and alcohol (*loc. cit.*), but it leads to a different mathematical expression for these substitution reactions.

The " 50% acetic acid " medium was selected for this first series of measurements because the value of the equilibrium constant for this medium at 18° has been determined by W. J. Jones (*loc. cit.*). An approximate value for K was also obtained from the velocity measurements. The values of x in a given reaction were plotted against t. The portion of the curve corresponding to 45—55% change is sensibly a straight line, hence the value of $\Delta x/\Delta t$ for this interval in the reactions with $b/a = 5$ and with $b/a = 10$, for each substance, was equated to the right-hand side of (1) and the two equations were solved for approximate values of K and k. The figures obtained are in Table I.

TABLE I.

Ether.	Approximate value of K.	k.
p-Chloroanisole	0·0208	0·659
p-Chlorophenetole	0·0212	1·46
p-Chlorophenyl *iso*propyl ether	0·0215	4·49
p-Bromoanisole	0·0209	0·685
p-Bromophenetole	0·0210	1·548
p-Bromophenyl *iso*propyl ether	0·0207	—

The mean value of K, *viz.*, 0·021, is in close agreement with the value 0·020 at 18° obtained by W. J. Jones by an aspiration method, and has been employed in the calculation of the velocity coefficients by means of equation (2). It will be seen (see Experimental) that constants for the velocity coefficients are given when b/a is 10, but that when it is only 5 there is a small but regular downward drift as the reaction progresses.

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It is not, of course, necessary to know the exact relation between the concentration of " unfixed " bromine and the composition of the solution to attain the main object of this investigation, *viz.*, a knowledge of the *relative* rates of the reactions. For if the differential equation be of the form

$$dx/dt = k\phi(C_{\text{ether}}, C_{\text{Br}_2}, C_{\text{HBr}})$$

where the C's represent concentration terms, the solution will be of the form

$$kt = \psi(C_{\text{ether}}, C_{\text{Br}_2}, C_{\text{HBr}})$$

For two reactions, when the initial concentrations are identical, at any given stage,

$$\psi(C_{\text{ether}}, C_{\text{Br}_2}, C_{\text{HBr}})_{\text{Reaction I}} = \psi(C_{\text{ether}}, C_{\text{Br}_2}, C_{\text{HBr}})_{\text{Reaction II}}$$

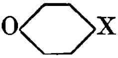
hence $k_1t_1 = k_2t_2$, *i.e.*, the ratio of the velocities is equal to the inverse ratios of the times taken for the reactions to proceed to any given extent. Since the necessary conditions were satisfied in these experiments, the velocity ratios were calculated from the times taken for 30%, 35%, etc., change, and were found to be constant within about 2%, as shown by the following typical example :

p-Chlorophenetole and *p*-Chloroanisole.

Change, % ...	30	35	40	45	50	55	60	65
$k_1/k_2 = t_2/t_1$ ...	230·6	228·1	229·7	228·4	227·3	227·6	227·0	230·2

In Table II are given the mean values obtained in this way for the velocities of (i) the ethyl and *iso*propyl ethers of *p*-bromo- and *p*-chloro-phenol (that of the corresponding methyl ether being taken as 100), and also of (ii) the three *p*-bromo-ethers (that of the corresponding *p*-chloro-ether being taken as 100).

TABLE II.

(i) Relative directive effects of the groups ·OR in compounds of the type ROX. Values of $100k^{\text{OR}}_{p\cdot\text{X}}/k^{\text{OMe}}_{p\cdot\text{X}}$.

	$b/a = 10.$			$b/a = 5.$		
R =	Me.	Et.	Prβ.	Me.	Et.	Prβ.
X = *p*-Cl	100	229	716	100	230	716
p-Br	100	231	709	100	233	704

(ii) Relative directive effects of the groups Cl and Br in compounds of the type ROX. Values of $100k^{\text{OR}}_{\cdot\text{Br}}/k^{\text{OR}}_{p\cdot\text{Cl}}$.

R =	Me.	Et.	Prβ.
$b/a = 10$	107	109	106
$b/a = 5$	108	109	105

An attempt to measure the relative rates of bromination in water of a number of organic substances has been made by Francis and his collaborators (Francis, Hill, and Johnston, *J. Amer. Chem. Soc.*, 1925, **47**, 2211; Francis, *ibid.*, 1926, **48**, 1631) by allowing two substances to compete for various quantities of bromine insufficient for complete bromination of both. Amongst the compounds examined were anisole and phenetole, but as the figures obtained by him have been subjected to "adjustments . . . averaging 15%," they must be regarded as qualitative only, and no useful comparison with the values now obtained can be made.

It has been shown (Bradfield and Jones, *locc. cit.*) that the relative rates of chlorination in 99% acetic acid of two ethers are independent of the proportion of ether to hydrochloric acid within the limits examined. Similarly, from Table II, it may be seen that the velocity ratio for a pair of ethers is the same for both concentrations of hydrobromic acid employed. Further, for chlorination at a fixed temperature, the ratios of the type $k_{p\cdot X}^{OR_1}/k_{p\cdot X}^{OR_2}$ are independent of the chemical nature of X, and those of the type $k_{p\cdot X_1}^{OR}/k_{p\cdot X_2}^{OR}$ independent of the nature of R, an experimental fact which has been interpreted as indicating that the energies of activation for the reaction between ethers and chlorine may be expressed as the *sum* of the characteristic individual contributions of the atoms or groups attached to the benzene ring, since, according to the activation theory of reaction velocity, the equation connecting the velocity coefficient with the energy of activation is exponential in form (Bradfield and Jones, *locc. cit.*).* Table II demonstrates a similar constancy of the ratios of the velocity coefficients for bromination in "50% acetic acid," and suggests a similar interpretation. Solubility considerations prevent a more extensive verification of these relations in this medium.

Preliminary experiments in other aqueous-acetic acid media show that the velocity of bromination of ethers, which is intrinsically smaller than the velocity of chlorination under corresponding conditions, increases rapidly with increasing water content of the medium.

EXPERIMENTAL.

Preparation of Materials.—The solvent consisted of a mixture of equal volumes of purified acetic acid, m. p. 16·0—16·2°, and water.

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* *Correction.* Since for a bimolecular reaction involving two *different* molecules the rate of reaction is reckoned as the number of molecules of *either* kind disappearing in unit time, in the expressions $k_0 = 2PSZe^{-E_0/RT}$, etc., the term Z represents the total number of collisions between the ether and halogen molecules and not double this number as stated in J., 1928, 1008. This correction makes no difference to the conclusions drawn, since, in using equations of this type, we have invariably cancelled the Z terms.

The bromine was shaken with dilute sodium hydroxide solution and then with concentrated sulphuric acid, and finally distilled from a little barium carbonate. The constant-boiling solution of hydrobromic acid employed was distilled over red phosphorus and preserved in the dark.

The ethers were prepared from the phenols and alkyl iodides in the usual manner and repeatedly crystallised, if solid, or distilled under 2 mm. pressure, if liquid. p-*Chlorophenyl* iso*propyl ether* distils with a bath temperature of 73—75°/1·5 mm., and has $n_D^{25^\circ}$ 1·5127 (Found : Cl, 20·9. $C_9H_{11}OCl$ requires Cl, 20·8%).

Method for Velocity Determinations.—Orton and King's method of chlorination (J., 1911, **99**, 1185), based on the reversible reaction between hydrochloric acid and a chloroamide, $>NCl + HCl \rightleftharpoons >NH + Cl_2$, was devised for kinetic measurements. Its eminent suitability aroused the hope, which has not, however, been entirely fulfilled, that either of the similar reactions (1) between a bromoamide and hydrobromic acid, $>NBr + HBr \rightleftharpoons >NH + Br_2$, or (2) between a chloroamide and hydrobromic acid, $>NCl + HBr \rightleftharpoons >NH + BrCl$ (yielding the active brominating agent bromine chloride) would prove equally serviceable for measurements of the velocity of bromination of appropriate aromatic compounds. There is a fair prospect of the successful application of reaction (2), but this communication deals only with efforts which have been made to measure the velocity of bromination when the substituting agent is the bromine molecule. A number of chloroamides are readily prepared as stable, well-crystallised substances, giving a solution in which an accurately known amount of chlorine can be generated at the required moment by the addition of hydrochloric acid. No bromoamide hitherto examined in these laboratories, however, has proved sufficiently stable to render its analogous employment as a source of bromine (reaction 1 above) superior to the use of a solution prepared by the addition of elementary bromine. The procedure adopted was as follows. A solution of bromine in "50% acetic acid," adjusted to contain as nearly as possible 0·0075 g.-mol. per litre, was standardised by titration with thiosulphate. 10 C.c. of this solution were pipetted into a solution of the weighed quantity of the ether in "50% acetic acid," to which the requisite amount of hydrobromic acid had been added, contained in a 200 c.c. graduated flask, all the solutions being at 20°. The solution was made up to the mark with "50% acetic acid," mixed by shaking, and placed in a thermostat at 20°. The time of mixing did not exceed 30 seconds, which is negligible with these slow reactions. From time to time 10 c.c. portions were withdrawn, run into potassium iodide solution, and titrated with $N/50$-thiosulphate. Later, it was found advantageous to incorporate a portion of the hydrobromic acid in the standard bromine solution, the resulting diminution of the partial pressure of the bromine (perbromide formation) facilitating its preservation at standard strength.

Calculation of Velocity Coefficients.—To assist calculation, the results of several determinations were plotted and values of *t* corresponding to 25%, 30%, etc., change were read from the smooth curve drawn through the points. Usually about 20 points were obtained for each curve, and individual points rarely deviated from the curve by more than the equivalent of 0·02 c.c. of *N*/50-thiosulphate. The velocity coefficients were calculated by equation (2) above.

Experimental Data.

$c = 0{\cdot}015$ throughout, and δ represents the extent % to which reaction has proceeded.

p-*Chloroanisole.*

$\left\{\begin{array}{l} a = 0{\cdot}007404. \\ b = 0{\cdot}0375. \end{array}\right.$

t.	δ.	*k.*
99·0	30	0·6942
123·5	35	0·6905
150·5	40	0·6851
183·0	45	0·6754
218·5	50	0·6739
260·7	55	0·6702
310·5	60	0·6639
367·5	65	0·6623
	Mean	0·677

$\left\{\begin{array}{l} a = 0{\cdot}007404. \\ b = 0{\cdot}075. \end{array}\right.$

t.	δ.	*k.*
169·0	30	0·6733
207·5	35	0·6696
255·0	40	0·6696
306·0	45	0·6662
364·0	50	0·6646
432·0	55	0·6628
514·0	60	0·6566
610·0	65	0·6512
	Mean	0·665

p-*Bromoanisole.*

$\left\{\begin{array}{l} a = 0{\cdot}007404. \\ b = 0{\cdot}0375. \end{array}\right.$

t.	δ.	*k.*
91·5	30	0·7511
114·5	35	0·7445
140·0	40	0·7365
169·0	45	0·7315
203·0	50	0·7255
242·0	55	0·7220
289·0	60	0·7133
345·0	65	0·7057
	Mean	0·729

$\left\{\begin{array}{l} a = 0{\cdot}007446. \\ b = 0{\cdot}075. \end{array}\right.$

t.	δ.	*k.*
157	30	0·7278
194	35	0·7234
237	40	0·7192
285	45	0·7170
340	50	0·7165
403	55	0·7100
479	60	0·7045
566	65	0·7027
	Mean	0·715

p-*Chlorophenetole.*

$\left\{\begin{array}{l} a = 0{\cdot}007298. \\ b = 0{\cdot}0375. \end{array}\right.$

t.	δ.	*k.*
42·7	30	1·609
53·5	35	1·587
65·3	40	1·574
79·7	45	1·548
95·2	50	1·543
114·2	55	1·525
136·0	60	1·514
159·0	65	1·528
	Mean	1·55

$\left\{\begin{array}{l} a = 0{\cdot}007298. \\ b = 0{\cdot}075. \end{array}\right.$

t.	δ.	*k.*
74·5	30	1·565
92·5	35	1·510
112·5	40	1·540
136·2	45	1·496
162·5	50	1·516
192·0	55	1·490
228·8	60	1·487
265·0	65	1·504
	Mean	1·51

p-*Bromophenetole.*

$\left\{\begin{array}{l} a = 0{\cdot}007404. \\ b = 0{\cdot}0375. \end{array}\right.$

t.	δ.	*k.*
38·8	30	1·772
48·9	35	1·744
60·0	40	1·718
72·5	45	1·706
87·5	50	1·683
104·7	55	1·669
124·5	60	1·656
148·5	65	1·639
	Mean	1·70

p-*Chlorophenyl* iso*propyl ether.*

$\left\{\begin{array}{l} a = 0{\cdot}007404. \\ b = 0{\cdot}0375. \end{array}\right.$

t.	δ.	*k.*
13·7	30	5·017
17·0	35	5·016
20·8	40	4·957
25·3	45	4·887
30·5	50	4·829
36·5	55	4·792
43·5	60	4·739
52·3	65	4·654
	Mean	4·86

p-*Bromophenyl* iso*propyl ether.*

$\left\{\begin{array}{l} a = 0{\cdot}007233. \\ b = 0{\cdot}0375. \end{array}\right.$

t.	δ.	*k.*
13·0	30	5·287
16·2	35	5·263
19·6	40	5·260
24·0	45	5·151
28·8	50	5·114
34·8	55	5·020
41·6	60	4·956
50·0	65	4·869
	Mean	5·12

p-*Bromophenetole.*

$\begin{cases} a = 0{\cdot}007404. \\ b = 0{\cdot}075. \end{cases}$

67·5	30	1·698
83·5	35	1·664
101·3	40	1·686
122·5	45	1·664
146·0	50	1·657
174·6	55	1·640
207·0	60	1·630
246·0	65	1·615
	Mean	1·66

p-*Chlorophenyl* iso*propyl ether.*

$\begin{cases} a = 0{\cdot}007404. \\ b = 0{\cdot}075. \end{cases}$

23·2	30	4·942
28·7	35	4·842
35·7	40	4·782
42·8	45	4·763
51·5	50	4·697
60·8	55	4·710
72·5	60	4·764
84·7	65	4·690
	Mean	4·77

p-*Bromophenyl* iso*propyl ether.*

$\begin{cases} a = 0{\cdot}007233. \\ b = 0{\cdot}075. \end{cases}$

21·8	30	5·261
27·3	35	5·131
33·3	40	5·116
40·3	45	5·047
48·5	50	4·990
55·5	55	5·146
68·4	60	4·910
81·3	65	4·890
	Mean	5·06

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